Letters to the Editor . . .

San Francisco

Editor, CALIFORNIA MEDICINE

Dear Sir:

On the jacket of Dr. Rudolf von Urban's book, "Sex Perfection and Marital Happiness," The Dial Press, Inc., New York, 1949, I found myself quoted as saying: "Based on an entirely new point of view, his experiences and theories will without doubt become the basis of a scientific research work."

This quotation may give the impression that I have reviewed the book of Dr. von Urban and that I have used the sentence in such a book review.

Therefore, I wish to state that the quotation obviously results from an error on the part of Dr. von Urban or his publisher.

Whatever the merits of Dr. von Urban's views are, I do not believe that his theories will become the basis of scientific research work in the future.

Very sincerely yours,

SIEGFRIED FISCHER, M.D.

Cytoplasmic Hereditary Determiner

Revision of the generally accepted mendelian theory of genetics is suggested by Sonneborn* of the department of zoology, Indiana University, based on rapidly accumulating evidence of the importance of extrachromosomal hereditary determiners, not taken into account in the present theory.

Much of this new evidence is drawn from a study of the hereditary characters of paramecia. For example, among the progeny of a common ancestor there may arise six antigenically different strains having identical nuclear genes. Each strain repeatedly injected into rabbits gives rise to a strain-specific antiserum. This serum is capable of paralyzing homologous-strain paramecia, but is nontoxic for other strains. Reciprocal crosses between paramecia of different strains show that the antigenicity is not determined by nuclear genes, since normal nuclear interchange does not alter the antigenicity of either conjugant. Under certain control conditions, however, atypical conjugation may take place. In such cases a cytoplasmic bridge is formed between the two conjugants and cytoplasm flows from one mate to the other. On separating, the two conjugants are now of identical antigenicity.

A second character studied by the reciprocal cross technique is the production of an ectotoxin ("paramecin") by certain "killer" strains. This toxin is lethal for certain "sensitive" paramecia but is nontoxic for homologous-type paramecia. Ordinary conjugation between killer and sensitive individuals, with normal nuclear interchange, does not alter the hereditary toxin production or sensitivity of either conjugant. With the cytoplasmic transfer of atypical conjugation, however, a sensitive conjugant which gets cytoplasm from a killer parent will multiply to produce a killer culture. A conjugant which receives cytoplasm from a sensitive parent produces a sensitive culture.

Extension of this cytoplasmic transfer to multicellular organisms has been deduced from studies of the hereditary CO_2-sensitivity or CO_2-resistance of fruit flies (Drosophila). If CO_2-sensitive and CO_2-resistant strains are mated reciprocally, the offspring are usually like the mother, CO_2-sensitive when she is sensitive and CO_2-resistant when she is resistant. This is interpreted as evidence of an hereditary transmission of CO_2-sensitivity or CO_2-resistance by means of ovarian cytoplasm, the sperm carrying practically no cytoplasmic material.

This interpretation has been confirmed microscopically. Killer paramecia usually contain from 200 to 1,000 cytoplasmic granules, or "kappa" particles, not demonstrable in sensitive paramecia. The rate at which kappa multiplies in a killer cell is independent of the rate of multiplication of the cell as a whole, and is determined or modified by such factors as temperature and food supply. When a killer paramecium divides, the kappa particles are usually distributed unequally between the two daughter cells. There may thus occur a marked increase in the number of kappa particles in one of the daughters, with a corresponding decrease in the sister cell. With an increase in kappa count there is a parallel increase in toxin production. With a moderately reduced kappa count there is a partial or complete loss of toxin production, but with retention of full toxin resistance or immunity. With a further loss of kappa particles, this immunity in turn is lost, the paramecium becoming sensitive or allergic to paramecin.

Since all cells of a multicellular animal are believed to contain the same set of nuclear genes, similar quantitative changes in cytoplasmic determiners are believed to be the key to the mechanism of cellular differentiation. Sonneborn believes such changes are also a key to the etiology of numerous organic diseases, including cancer.

On disintegrating, killer paramecia set free kappa particles into the environment. Non-killer paramecia exposed to this environment may ingest, and thus acquire, killer genes, and give rise to a new killer strain. The kappa particles thus have properties similar to those of a non-pathogenic or even beneficial virus.

Future studies of kappa particles and other cytoplasmic hereditary determiners may therefore be of basic clinical interest.

W. H. MANWARING
Stanford University, Calif.

*Sonneborn, T. M.: Amer. Scientist, 37:33 (Jan.), 1949.